# ALASKA MEDICAID
# PHARMACY AND THERAPEUTICS COMMITTEE

**Location of Meeting**
**Frontier Building, 3601 C Street, Room 890/896**

**MINUTES OF MEETING**
**November 17, 2006**
**8:00 a.m.**

**Committee Members Present:**
Marvin Bergeson, MD
Heidi Brainerd, MS, RPh (telephonic)
Amber Briggs, PharmD
Richard E. Brodsky, MD
Lucy Curtiss, MD
Kelly Conright, MD
Jeffrey G. Demain, MD
Traci Gale, RPh (telephonic)
R. Duane Hopson, MD
Thomas K. Hunt, MD
Ronald Keller, MD
Diane Liljegren, MD (telephonic)
Gregory R. Polston, MD
Sherrie D. Richey, MD
Janice L. Stables, MSN, ANP
Trish D. White, RPh (telephonic)

**Committee Members Absent:**
Robert Carlson, MD
Vincent Greear, RPh
Andrzej Muciejewski, MD

**Others Present:**
David Campana, RPh
Melinda Sater, PharmD, First Health
Alexander VonHafften, MD

## 1. Call to Order – Chair

The meeting was called to order at 8:00 a.m.

## 2. Roll Call

A quorum was present.

## 3. Public Comment – Local Public/Local Physicians

**Dr. Vern Stillner**: As a Medicaid practitioner (no audio).

**Dr. Mary Hillstrand**: (No audio.)

**Dr. Mary Down**: An Anchorage neurologist discussed Alzheimer medications, Aricept and Exelon, both of which are currently on the PDL. Aricept is easy to use, dosed once a day and has good compliance. Exelon has no drug interactions and is very safe. A recent study shows that patients that are declining on Aricept can have stabilization or improvement when switched to Exelon. It is also approved for Parkinson dementia. Aricept and Exelon are both very important and should remain on the PDL. (No audio during questions.)

**Dr. Mary Hillstrand**: Agreed with Dr. Mary Downs. The multiple sclerosis medications are very important in decreasing disabilities in young women between the ages of 20 and 40. All of the medications decrease disabilities between 40-50%. Long-term care for multiple sclerosis patients is expensive, but their outcome is improved when on medication. I use Rebif the most, but some patients cannot tolerate interferons and have to be put on Copaxone.

**Dr. Charles Burgess**: A psychiatrist at the Homer Community Mental Health Center primarily discussed Alzheimer medications, but agreed with Dr. Vern Stillner regarding antidepressants. Donepezil is the most important tool in my toolbox for treating Alzheimers. We are at the verge of a critical time in Alaska, because of the huge influx of retirees coming into the state. Currently, there are about 2,500 people between the ages of 65 and 75 who have dementia. Of those between the age of 75 and 80, about 50% will have dementia. The tools in our toolbox are limited, so we value the ones we have. Donepezil is well tolerated and has once-a-day dosing. Its ability to preserve the patient's function is enough that the cost/benefit ratio is a no-brainer. Tolerability, efficacy, and the ability to improve patient functions are critical in the care of Alzheimer patients.

In response to Dr. Hunt, Dr. Burgess said having only one of these drugs on the PDL would not hamper his practice. Donepezil is clearly the most favored Alzheimer drug in the state, primarily due to its tolerance. Memantine is his second choice. The committee needs to look at the challenging issue of using A-typical antipsychotics in elderly people. These drugs have proven efficacy for limiting episodes such as one patient assaulting another or a patient getting up and wandering out of the house in the middle of the night. One criticism I hear is that these medications do not improve memory. It is important to remember that these drugs are not necessarily memory enhancers, but they preserve ADLs, function, and engagement, which is a critical factor in terms of workability with caregivers and other people around Alzheimer patients.

Dr. Brodsky reminded the representatives from the pharmaceutical companies that there was a proper submission procedure. The submission form and the deadlines are posted on the website. Submissions will not be accepted at the meetings.

## 4. Re-review of the Other Antidepressants

There were no public testimonies.

Dr. Sater gave the First Health presentation on Other Antidepressants. This is a very diverse classification. There are six available chemical entities and many different products. The mechanisms differ slightly, or in some cases drastically, between the agents. The adverse drug reactions vary between the agents. In clinical trials and reviews, the efficacy has been shown to be similar among all the agents. In October of 2006, there were 2,884 claims as follows: generic Trazodone, 27%; Effexor XR, 21%; Wellbutrin XL, 18%; Cymbalta, 16%; generic Wellbutrin, 6%; Mirtazapine, 6%; other generic Wellbutrin products, 1%; and the rest were less than 2% all total. In previous discussions, the difficulty in categorizing this varied group of drugs together was discussed. Drs. VonHafften and Sampson stated once daily dosage forms should be included on the PDL. After several amendments, the motion was made to include all antidepressants, in at least their extended release formulation, on the PDL. Wellbutrin SR and XL were specifically included, as was the 60-day grandfathering of patients previously stabilized on drugs in this class. The motion passed unanimously. Since the last review, Venlafaxine immediate release has become available as a generic. The box warning about the use of this class of drugs in children and teenagers has been added to the labeling.

Dr. Polston said Trazodone was very important for sleep in the patient population with pain. Cymbalta is being used in this population, because it is often difficult to differentiate between depression and pain. Effexor is a medication that has been used long-term.

Dr. Curtiss agreed with the other psychiatrists that in her practice the long-acting drugs had better adherence and response.

Dr. Sater said not all brands and generics were preferred, but all dosage forms of the chemical entities available at the time were preferred. Only Wellbutrin XL was specifically preferred.

Dr. Hunt thought they had worded the motion to insure that all agents were listed.

Dr. Sater said the meeting minutes said, "The motion was made to include all antidepressants in at least their extended release formulation."

**DR. HUNT MOVED TO INCLUDE ALL ANTIDEPRESSANTS IN AT LEAST THEIR EXTENDED RELEASE FORMULATION. SECONDED BY DR. BERGESON.**

Dr. Demain said he and Dr. Sater participated in a symposium that discussed drugs that received black box warnings and had specific concerns regarding children. One of the topics was how important these warnings were for children. He felt a drug preference for children should to be discussed.

Dr. Bergeson suggested including Effexor and Wellbutrin, which are used not only for depression, but also for ADD, substance abuse, and pain. Trazodone is a very important drug for pediatrics. He did not believe there was a class effect in this group, because of the different effects and purposes of the drugs. He felt all of the class should be represented, especially in the long-acting forms, as well as Wellbutrin and Effexor.

Dr. Demain pointed out that the generic forms of Bupropion were prescribed less than 1% of the time.

Dr. Curtiss said the generic forms of Bupropion were short-acting drugs, so people tend to have more side effects and do not take their doses later in the day.

Dr. Sater said two of the generic Wellbutrin products listed are SR products were dosed twice daily.

Dr. Curtiss said there was a difference between Wellbutrin XL and SR in her practice. The XL is clearly more effective.

Dr. Hunt suggested adding the branded Wellbutrin XL to the PDL.

**DR. HUNT AMENDED THE MOTION TO INCLUDE EVERY CHEMICAL ENTITY REPRESENTED, ALL AVALABLE EXTENDED RELEASE PRODUCTS, AND BRANDED WELLBUTRIN XL. DR. BERGESON ACCEPTED THE AMENDMENT.**

Dr. Richey pointed out that the conclusion in the packet says there are no statistically significant differences in the classification, but based on our clinical experience, we want to have these drugs on the PDL. This is probably opposite of what we will do in the next classification.

Dr. Liljegren said that although statistically they all look the same, we are acknowledging that individuals are not statistics.

Dr. Richey agreed with Dr. Liljegren, but was simply pointing out the committee's internal inconsistencies regarding different classes of drugs.

Dr. Conright said in a prior meeting Dr. Hunt had asked for clarity in the definition of class effect. If we are strictly keeping the class effect comment to the treatment of depression, we could say it is a class effect. However, these medications have secondary indications.

Dr. Hunt said the committee's inconsistency also concerned him. He discussed how studies were generally conducted. It would be feasible for the committee to insist that the state have no preferred agent for new starts, in other words choose one drug according to the bidding process. If the new start failed, you would write medically necessary to prescribe something else. However, in classifications that are widely prescribed, it would be easier to allow multiple drugs in the classification.

Dr. Richey said the committee's charge was not to make it easy for the practitioners. We need to insure that the Medicaid population is not discriminated against and they have easy access to appropriate drugs. Our charge is not the cost issue. Our charge is to clinically evaluate the data and make recommendations.

Dr. Bergeson said this group of drugs was largely used off label, not only for depression, and needed to be available to practitioners for those other purposes.

Dr. Brodsky said all the committee could do was make the best choices possible. Cost is always in the backs of our minds. The bottom line is the state is trying to save money so we can provide the best care possible for the Medicaid population.

The committee discussed the consistency of the committee's decisions.

**THE MOTION PASSED WITH TWO OPPOSED.**

## 5. Re-review of Ophthalmic Immunomodulators

There was no public testimony.

Dr. Sater gave the First Health presentation on Ophthalmic Immunomodulators. In this class there is only one available agent, Restasis. It is approved for the treatment of keratoconjunctivitis sicca, or dry eye disease. In October 2006 there were 12 claims. When the drug was previously reviewed, there was no discussion. The motion was the prefer Restasis and it passed unanimously. Dr. Nybor believes that Restasis is a significant therapeutic advance for a condition that previously had no treatment available. Prior to Restasis, only symptomatic management measures were used. He felt the drug had minimal, if any, side effects. Dr. Robert Arnold, however, does not see a role for Restasis in his pediatric setting.

Dr. Brodsky said Dr. Robert Werner felt Restasis was a good drug when used appropriately, but it tends to be over used and prescribed for everyone who complains about dry eyes.

**DR. POLSTON MOVED TO PREFER RESTASIS. SECONDED BY DR. DEMAIN. THE MOTION PASSED WITH TWO OPPOSED.**

## 6. Re-review of Ophthalmic Antihistamines

**Mr. Mike Jensen**: Discussed the drug Elestat. The ideal drug therapy for allergic conjunctivitis should provide treatment for total antihistaminic activity at both the H-1 and H-2 receptors, mast cell stabilization, and a drug with anti-inflammatory properties is considered a more ideal drug. Unlike the other topical antihistamines currently on the PDL, Elestat is unique in that it provides activity at not only the H-1 receptor, but it is the only topical antihistamine product to be identified that also provides activity at the H-2 receptor. Elestat provides complete and comprehensive treatment through a multi-action effect. It is a proven mast cell stabilizer. In our current practice, Elestat is one of the most rapidly acting agents on the market, providing symptomatic relief in as fast as three minutes and a sustained duration of activity for up to 12 hours. It can also be dosed twice daily on a 12-hour basis, an advantage over other agents that might require more frequent dosing such as every 6-8 hour or 8-12 hours. The dosing helps in patient compliance and requires fewer refill needs over time. Elestat is very well tolerated. It also provides a similar safety profile with the other agents currently on the PDL for use in children and it is safe for children three years of age or older. Elestat has widely become accepted as an important agent nationwide in the treatment of allergic conjunctivitis. Having access to Elestat would greatly benefit Alaska Medicaid patients and improve their treatment of allergic conjunctivitis.

Dr. Sater gave the First Health presentation of Ophthalmic Antihistamines. There are seven available agents, all approved for allergic conjunctivitis. Emadine and Livostin have selective H-1 receptor

activity. Elestat, Optivar, Patanol and Zaditor have mast cell stabilization and histamine receptor, as well as other mechanisms. Acular and Alrex are anti-inflammatories. Head to head trials are often limited by comparing agents with a single mechanism of action versus agents that have multiple mechanisms, the difference in measuring and defining outcomes or the study design. In October 2006, there were 64 claims as follows. Patanol, the currently preferred agent, had 98% market share. There was one claim for Zaditor. There was significant discussion previously regarding clinical efficacy and superiority from clinical evidence versus antidotal evidence. The motion to include Patanol for all ages failed. The motion to consider these agents equivalent, except to prefer Patanol for those under 12, passed with nine in favor and seven opposed. There have been significant changes in this class. In the first half of 2007, Zaditor will be available as an OTC product. Dr. Robert Arnold prefers Patanol in his practice. He said the dual mechanism of action is desirable, especially when treating severe allergic conjunctivitis. He feels this medication is the one used most appropriately by community practitioners as well. Dr. Nybor also prefers Patanol.

Dr. Demain said he preferred Patanol, based on use and patient tolerability. This drug has had head to head studies with the other drugs and has consistently shown superiority in control of symptoms and patient tolerability. He noted that 98% of the prescription in 2006 had been for Patanol.

**DR. DEMAIN MOVED THAT THIS IS A CLASS EFFECT WITH A PREFERENCE FOR PATANOL FOR ALL AGES. SECONDED BY DR. BERGESON.**

Dr. Bergeson felt although there was a class effect, Patanol was a superior drug.

The committee discussed the seasonal nature of these drugs and the possible need to review more than a single month's worth of prescriptions. They also discussed the number of physicians prescribing these drugs in relation to how easy or hard it might be to change the preferred drug.

**THE MOTION PASSED UNANIMOUSLY.**

### 7. Re-review of Mast Cell Stabilizers

There were no public comments.

Dr. Sater gave the First Health review of Mast Cell Stabilizers. There are four available agents and they are all approved for allergic conjunctivitis in one form or another. This particular class of drugs offers no real benefit in the treatment of acute allergic conjunctivitis. In October 2006, there were three claims. At the last review there was no discussion. The motion that this be considered a class effect passed unanimously. There have not been any real changes in this class since the last review. The preferred agents are generic Cromolyn and Alocril. Dr. Arnold does not see any particular clinical utility for any agent in this class; he prefers Patanol. Dr. Nybor does not have a preference in this class.

**DR. BERGESON MOVED THIS IS A CLASS EFFECT. SECONDED BY DR. HUNT. MOTION PASSED UNANIMOUSLY.**

## 8. Re-review of Ophthalmic Quinolones

**Mr. Mike Jensen**: Recommended Zymar for the PDL. The types of infection should determine the appropriate antibiotic use of topical antibiotics, particularly quinolones. Non-vision and non-threatening infections are typically self-limiting infections most often caused by viruses. It is cheaper and better to use less expensive and well-tolerated drugs, not only too decrease preventing possible drug resistance, but also to help decrease the cost to the patients and formularies for healthcare plans. Vigamox is probably the most frequently used and prescribed form of quinolones in Alaska. Its widespread use is associated not necessarily with greater efficacy, but because it is aggressively promoted in inappropriate arenas such as pediatrics. It is important to reserve these antibiotics for more serious and vision threatening infections. For those types of situations, we require broader spectrum antibiotics with better penetration, less resistance risk, and lower MIC-90s that are able to properly treat severe bugs. No other drug class, other than the fourth generation quinolones, meet this criterion. Multiple studies have been done on these drugs comparing them head to head. Trials suggest that Zymar is better tolerated in patients. Zymar contains a preservative, which has a faster kill rate than Vigamox. Zymar has less risk of contamination and is shown to be safer, faster and less toxic in corneal healing rates, as demonstrated in a study. Zymar was shown to be superior to Vigamox in 48 corneal transplant patients. There has been recent information published in the American Journal of Health System Pharmacy 2006 that reported 18-month data looking at infection rates and comparing Zymar and Vigamox. Both were equally efficacious in infectious rates, but Zymar was better tolerated in patients and actually saved money for the health plans and institutions using the drug. Vigamox is often over utilized, due to its strong promotion in the pediatric arena. It is important to consider patient tolerabilities and the importance of preserving antibiotics due to increasing infectious rates. Placing Zymar on the formulary as an alternative would benefit Alaska Medicaid patients and help control the use in the pediatric and primary care arenas.

**Mr. Eric Burns**: Spoke on behalf of Vigamox. In response to the previous speaker, he reviewed the utilization of the drugs in this class and concluded that there is appropriate utilization. The company that manufactures Zymar also promotes its products to primary care physicians. You want the highest concentration and the most potent antibiotic on the injection site. Since you are not going through the circulatory system, but into a closed organ, you are able to achieve hundreds-fold higher concentration of antibiotic to the site, like dropping a bomb on the infection that kills all the bacteria. Literature points to the use of these medications to thwart resistance, particularly to the older generation flouoroquinolones that require one mutation for resistance to occur. For tolerability and efficacy, the data shows that Zymar and Vigamox are therapeutically equivalent.

Dr. Sater gave the First Health presentation on Ophthalmic Fluoroquinolones. There are five available agents. All of the agents are indicated for bacterial conjunctivitis. Ciloxan and Ocuflox are indicated for corneal ulcers as well. All the agents have similar adverse effect profiles and efficacy. Currently, Vigamox and Ciprofloxacin drops are preferred. In October there were 251 claims: Vigamox, 52%; Ciprofloxacin drops, 19%; Ofloxacin drops, 19%; Zymar, 6%; Ciloxan drops, 6%; and 1 claim for Quixin. In previous discussions, there were significant talks about restricting use of this class and encouraging providers not to use these drugs. Concern about resistance was stated. The motion to consider these drugs therapeutically equivalent passed unanimously. There have been no significant changes in this class since the last review. Dr. Nybor uses primarily Zymar for his laser surgery

patients. He sees the small package size of Vigamox as a potential disadvantage, but states that both are excellent drugs. Dr. Arnold said Vigamox and Zymar were his preferred agents and have equal efficacy. However, he related a story about a child that was less than a year old and had two corneal transplants. He felt Vigamox was better tolerated by the child and the taste, when the drop run down the face into the mouth, was more favorable, possibly due to the lack of preservatives.

Dr. Brodsky said Dr. Werner felt they were all equivalent. The drugs are appropriate for corneal ulcers and other vision threatening conditions, but are over used for people with self-limiting conditions.

**DR. BRIGGS MOVED THAT THIS IS A CLASS EFFECT. SECONDED BY DR. DEMAIN.**

Dr. Briggs said she was unclear on the process for restricting use. A local pediatrician recently attended a conference where they were pushing Vigamox and said she would not be using Polytrim anymore and would use Vigamox exclusively.

Dr. Hunt did not believe use should be restricted, because there are cases that are eye threatening.

**THE MOTION PASSED UNANIMOUSLY.**

### 9. Re-review of Non-Ergot Dopamine Receptors

**Dr. John Robinson**: Parkinson's disease is a progressive neurodegenerative disease with debilitating and devastating motor and non-motor symptoms. The annual incidence of Parkinson's disease in North America is about 20 per 100,000 people. Parkinson's disease affects about one million people in the United States. The estimated economic burden attributed to Parkinson's disease is about $25 billion per year. Mirapex is rapidly absorbed in about two hours. No dosage adjustment is necessary in patients with hepatic insufficiency, as urinary excretion is the primary route for Mirapex's elimination. Dosage adjustments are required for patients with renal failure. Mirapex has a flexible dosing with ease of titration. Rapid titration may be achieved to an effective dosage of 1.5 to 4.5 milligrams per day in three divided doses. This is administered over three weeks in patients with normal rental function and with or without Levodopa. Mirapex has been a therapy in early diseases and has helped to improve motor function and activities of daily living. It has also helped to delay the onset of motor complications and the need for Levodopa. Mirapex, as an adjunctive therapy, has helped increase the duration and quality of on time, as well as reduce the duration and severity of off time. It has helped to improve tremors and reduce the Levodopa dose. He reviewed Mirapex's safety and tolerability. Patients have reported falling asleep without perceived warning signs during activities of daily living, including operation of a motor vehicle, which sometimes resulted in accidents. Hallucinations and postural or orthostatic hypertension may occur. Patients and caregivers should be informed about impulse control disorders and compulsive behaviors that may occur while taking medications to treat Parkinson's disease. Mirapex is well tolerated in early and late Parkinson's disease. There are no predicted P-450 interactions. It is renally cleared and no adjustment of dosage is required in patients with normal renal function. The use of Mirapex in Parkinson's disease has been shown to be efficacious to help treat the motor symptoms of Parkinson's disease, to help improve activities of daily living, to help delay the onset of motor complications, and to reserve the use of Levodopa until patients need it most.

Facilitating access to Mirapex will allow the State of Alaska to provide physicians and patients with an effective and safe agent for the treatment of Parkinson's disease.

**Dr. Jennifer Brzana**: Ropinirole has demonstrated safety and efficacy as an initial monotherapy in early Parkinson's disease (PD), as well as an adjunctive therapy in late PD. Ropinirole was the first FDA approved treatment for moderate to severe primary restless leg syndrome with symptomatic improvement in as early as two nights of treatment continued to nine months. Published data on Requip for the treatment of RLS exceeds all other dopamine agonists. Ropinirole tablets come in multiple strengths, offering flexible dosing in a wide therapeutic range, to allow clinicians to adjust therapy to meet the needs of patients with Parkinson's disease, as well as RLS. Levodopa has long been considered standard therapy for Parkinson's disease. However, long-term use of Levodopa can be associated with debilitating adverse motor fluctuations, as well as dyskinesias. Because dopamine agonists provide symptom improvement and a low risk of dyskinesias compared to Levodopa, treatment guidelines for PD recommend dopamine agonists as the first line initial monotherapy in newly diagnosed Parkinson patients, as well as adjunctive therapy to Levodopa. A five-year study with Ropinirole showed that newly diagnosed Parkinson patients had fewer dyskinesias when treated with Ropinirole compared to Levodopa monotherapy. Also in studies of patients with advance disease already on Levodopa, the adjunctive therapy with Ropinirole resulted in not only a reduction in total Levodopa dose, but it also helped to reduce awake time spent with increasing Parkinson symptoms, compared to placebo. Restless leg syndrome is a highly prevalent debilitating syndrome affecting about 10% of the population. These patients experience this unrelenting urge to move their legs, accompanied by uncomfortable sensations. It generally occurs especially early in the disease, late in the evening during periods of rest or inactivity. This can result in significant impact on sleep.

According to the treatment developed by the Restless Leg Syndrome Foundation and published in 2004, dopamine agonists are considered first choice in patients with daily RLS symptoms. Published data supporting Requip for the treatment of RLS includes over 1,000 patients. These studies show significant improvements in RLS scale scores and clinical global improvement after two doses. A 36-week trial evaluating Requip versus placebo found that significantly more patients treated with Ropinirole maintained a positive response throughout the nine-month period. Ropinirole is well tolerated. Ropinirole is the first FDA approved treatment for moderate to severe primary RLS with efficacy evident after two doses, continued through nine months. Ropinirole has demonstrated safety and efficacy in the treatment of Parkinson as initial monotherapy in early PD and as an adjunctive therapy to Levodopa in advanced PD. Multiple strengths of Requip allow clinicians to titrate therapy to meet the needs of both RLS and PD patients. These three points allow Ropinirole to stand alone in the class of dopamine agonists and make it a clear choice for the preferred agent on the Alaska State Medicaid PDL.

In response to Dr. Hunt, Dr. Brzana discussed the treatment of restless leg syndrome. Secondary restless leg syndrome can be due to iron deficiency. In patients with iron deficiency, about 30 percent will manifest symptoms of restless leg syndrome. In those patients, treating the iron deficiency is the treatment of choice. Oftentimes, although iron therapy in that subset of patients with secondary RLS is preferred, they often need symptom treatment as their iron level is being increased.

Dr. Sater gave the First Health presentation on Non-Ergot Dopamine Receptors. There are two available products, both of which are FDA approved for the treatment of Parkinson's disease. Requip is indicated

for the treatment of RLS, although both have been studied and used for the indication. There are similar pharmacokinetic profiles and clinical efficacy between the two drugs. Requip may have an increased incidence of hypertension. Mirapex may be associated with increased risk of hallucinations. Head to head comparative trials are limited with drugs in this class. In October, there were 131 claims: Mirapex, 56%; and Requip, 44%. Both drugs are currently preferred. At the last review, there was a short discussion regarding therapeutic equivalence. The motion was made to consider this a class effect and passed unanimously. Dr. Jeffrey Sponslor primarily uses Mirapex, but considers the agents equivalent.

**DR. BRIGGS MOVED THIS IS A CLASS EFFECT. SECONDED BY DR. BERGESON. THE MOTION PASSED UNANIMOUSLY.**

**10. Re-review of Multiple Sclerosis Agents**

**Dr. Lori Howarth**: The Berlex product, Betaseron, is one of the foremost commonly used agents to treat multiple sclerosis. Betaseron was approved by the FDA in 1993 and has 16 years of clinic data. Betaseron is a high dose, frequently administered interferon. In 2002, the American Academy of Neurology published its consensus report on disease modifying therapies in the treatment of multiple sclerosis. Reviewing the pivotal trials and using an evidence-based medicine approach, the AAN offered a set of guidelines based on their evidence-based analysis that higher and/or more frequent dosing results in more successful outcomes. Since Betaseron was the first interferon to be approved, we have the longest amount of data. We just performed a 16-year long-term follow-up study that showed Betaseron was well tolerated over the long-term with high adherence rates and mean treatment duration of over 10 years. After 16 years, it was possible to identify close to 90% of the patients from the original pivotal trial. Treatment with Betaseron was associated with a slower Expanded Disability Status Scale (EDSS) progression. The EDSS was delayed by six years in those treated with Betaseron for greater than 80% of the time as compared to those treated for less than 10% of the time. Betaseron has the longest evaluation of clinical efficacy of any interferon in multiple sclerosis. Several studies were reviewed. Betaseron is a high-dose, frequently administered interferon, which according to the AAN guidelines, leads to more successful outcomes. It has 16 years of clinical data that shows a delay in EDSS progression. Betaseron should be included on the PDL.

Dr. Sater gave the First Health review of Multiple Sclerosis Agents. There are four available products, all of which are FDA approved for the treatment of relapsing forms of MS. They have similar clinical efficacy. Avonex and Rebif may have less formation of neuralizing antibodies. Copaxone is not an interferon. It modulates the immune response through a different, and not fully understood, process. In October there were 22 claims: Rebif, 32%; Avonex, 27%; Copaxone, 27%; and Betaseron, 14%. All the drugs are currently preferred. Previous discussion mostly centered around access to drugs, including a grandfather clause and the importance of having one interferon product and Copaxone on the PDL. The original motion was that one interferon and Copaxone be added to the PDL, with the interferon considered therapeutically equivalent, was amended to include a grandfather clause, and then passed unanimously. There have not been any significant changes to this class since the last review. Dr. Sponslor uses all drugs in this class, but said the choice of the initial agent is very individualized and all drugs should be available.

Dr. Brodsky said Dr. Gordon agreed that one interferon, as well as Copaxone, should be on the PDL and the initial prescribed agent was very individualized.

Dr. Hunt said if the drugs appear to be clinically equivalent, one should not be preferred over the other.

The grandfather clause was discussed. Dr. Briggs felt writing medically necessary was sufficient due to the limited number of claims in this class.

Dr. Richey pointed out that although people have testified that these drugs should be available on the PDL, the committee has decided not to make a motion that it is a class effect, which is inconsistent with what was done earlier today.

Dr. Hunt pointed out that these drugs were the same, just different delivery systems.

**DR. HUNT MOVED THAT THE INTERFERONS WERE THERAPUTICALLY EQUIVALENT AND ONE INTERFERON AND COPAXONE SHOULD BE PERFERRED. SECONDED BY DR. KELLER. THE MOTION PASSED WITH ONE OPPOSED.**

**11. Re-review of Cholinesterase Inhibitor - Alzheimer**

**Mr. Matt Born**: Exelon is currently on the PDL and should remain there. Exelon is indicated for the treatment of mild to moderate dementia associated with Alzheimer's disease, as well as Parkinson's disease. The approval of Exelon in Alzheimer's disease was based on data generated by clinical studies involving over 2,700 patients enrolled in one of four separate clinical trials, as well as from data from numerous uncontrolled safety studies. Efficacy was demonstrated in studies that evaluated three key domains used to assess the disease: activities of daily living, behavior, and cognition. Exelon was shown to have statistically significant and clinically relevant benefits in all three of these areas. On June 28, Exelon became the first and only cholinesterase inhibitor approved for the treatment of mild to moderate Parkinson's disease dementia or PDD. PDD is characterized by impairments in executive function, memory retrieval and attention in patients with an established diagnosis of Parkinson's disease. The FDA's approval was based on results from a large-scale controlled study of over 500 patients demonstrating statistically significant improvement in the cognitive symptoms seen in PDD with Exelon versus placebo. The safety and tolerability of Exelon have been widely studied in clinical trials. Exelon is safe and appropriate for use with a wide variety of medications, based on a lack of drug-drug interactions with many commonly prescribed drugs, which is important because on average, elderly patients take between four and five medications daily and those in nursing homes may take has many as 12 daily. Due to its favorable pharmacology and lack of need for dose adjustment in renal or hepatic failure, Exelon can be administered safely in patients with Alzheimer's or Parkinson's disease dementias who are receiving other medication. The most common adverse events reported during the clinical trials were primarily those expected with the administration of cholinesterase inhibitors including nausea, vomiting, anorexia and others. These adverse events were generally mild to moderate in intensity, transient and self-limiting, and were most often observed during the forced titration phase of the studies. As with other cholinesterase inhibitors, weight loss was also observed with the treatment of Exelon.

Despite the elevated incidents of the most common adverse events such as nausea and vomiting, the discontinuation rate associated with these adverse events was relatively low. The inflexibility of the dose titration paradigm in the maximum tolerated dosage design employed in these studies appear to have artificially increased the incidents of adverse events, especially during the titration phase. Subsequent studies with slower titration rates and increased dosing flexibility demonstrated improved tolerability as evidenced by lower discontinuation rates. Exelon is commercially available in two dosage forms, oral capsules and oral liquid, offering ease of use and flexibility. Exelon should be retained on the PDL.

**Mr. Christopher Conner**: Reviewed a report from a state government supported evidence-based practice center in Oregon. Aricept is the only Alzheimer's agent that was looked at in head-to-head studies that was able to show a statistically significant difference with respect to cognitive scales. The adverse events and dropout rates were lowest with Aricept. On October 13, 2006, the FDA approved the use of Aricept in the treatment of severe Alzheimer's disease. Aricept is the only drug in this group that has an indication across all the different severities of Alzheimer's disease. In addition to the efficacy, tolerability and indications, the titration regimens are important to look at. If you cannot titrate these agents in their optimal dose ranges then you are not likely to see the kind of efficacy that is reported in the evidence-based literature. When you compare these agents, Aricept has the most simple titration regimen. In reviewing the first and second quarter data for Alaska, I saw some trends that indicated that Alaska was not getting patients titrated to effective doses with some of the other agents. With Aricept, you start at an effective dose of 5 milligrams with only one titration needed to get to the maximum effective dose of 10 milligrams. Due to the efficacy and tolerability evidence, as well as the fact that it is the only agent within the class that is approved across all the different severity levels of the disease, Aricept should be available on the PDL.

Dr. Sater gave the First Health report on Cholinesterase Inhibitors-Alzheimer. There are five available agents in this class. (Microphone button not pressed.) Cognex is not recommended for use, because of minimal effects. Exelon has a significant interaction with food, although no drug interactions are noted. Exelon and Aricept are both currently preferred, as is Namenda. The recommendation of this committee was to consider those separately. There were 55 claims for Namenda in October, and 86 for the remainder of the class, of which 84 were for Aricept and 2 for Exelon. Previous discussions related primarily to equal but limited efficacy of drugs in this class. Namenda was considered separately. The motion to consider the class therapeutically equivalent, but preferentially exclude Tacrine, passed unanimously. The motion to prefer Namenda passed with one opposed. Dr. Sponslor uses Aricept and Namenda in combination. He feels that the combination has better efficacy than either agent alone.

Dr. Demain reviewed the adverse reactions rates on page 11. There seemed to be a significant decrease in side effect profiles and adverse reaction rates, and therefore decreased dropout rates, with Aricept.

**DR. HUNT MOVED TO CLAIM THE CHOLINESTERASE INHIBITORS AS EQUALLY EFFECTIVE, INCLUDE NAMENDA, AND INSURE THAT COGNEX IS NOT ON THE PDL. SECONDED BY DR. CONRIGHT.**

Dr. Demain felt there was enough testimony to support considering Aricept as a preferred drug.

**THE MOTION PASSED WITH TWO OPPOSED.**

## 12. Final Comments by Chair or Other Members

Mr. Campana said Pharmacist Mark Bohrer from Fred Myers would be joining the committee at the next meeting.

Dr. Brodsky said there were still a dentist and possibly an OB slot to be filled.

Dr. Malter, the new medical director for Medicaid, introduced himself and said he had been asked to participate in the committee. However, he felt the committee was doing a great job and he would only monitor the committee at this time.

Dr. Sater reviewed the changes made to the PDL at this meeting.

- Other Antidepressants: Trazodone, Effexor XR, Wellbutrin XL, Cymbalta, generic Wellbutrin immediate release and SR, generic Mirtazapine products, Effexor immediate release and generic Nefazodone.
- Cyclosporine Ophalmic: Restasis.
- Ophthalmics for Allergic Conjunctivitis: Patanol.
- Mast Cell Stabilizer: Generic Cromolyn.
- Ophthalmic Fluoroquinolones: Vigamox and Ciprofloxacin drops.
- Antiparkinson's Agents: Mirapex and Requip.
- Multiple Sclerosis Agents: All MS agents will remain preferred.
- Alzheimer's Agents: Aricept, Exelon and Namenda.

## 13. Meeting Minutes

The committee reviewed the October 13, 2006 meeting minutes and made several changes.

**DR. BERGESON MOVED TO APPROVE THE OCTOBER 13, 2006 MEETING MINUTES, AS AMENDED. SECONDED BY DR. DEMAIN. THE MOTION PASSED UNANIMOUSLY**.

The committee reviewed the September 15, 2006, meeting minutes and made several changes.

**DR. BERGESON MOVED TO APPROVE THE SEPTEMBER 15, 2006 MEETING MINUTES, AS AMENDED. SECONDED BY MS. STABLES. THE MOTION PASSED UNANIMOUSLY.**

Dr. Sater said the next meeting would be January 19, 2007.

Dr. Brodsky adjourned the meeting at 10:34 a.m.